PATENTS

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of

Mohamed CHOKRI et al.

BOX AF

Serial No. 09/304,564

GROUP 1642

Filed May 4, 1999

Examiner A. Holleran

MACROPHAGES, PROCESS FOR PREPARING THE SAME AND THEIR USE AS ACTIVE SUBSTANCES OF PHARMACEUTICAL COMPOSITIONS

RESPONSE AFTER FINAL REJECTION

Commissioner for Patents
Washington, D.C. 20231

Sir:

Responsive to the final Official Action of March 27, 2001, applicants respond as follows.

Claims 3-5 are pending with claim 3 being independent.

The Official Action rejected claims 3-5 under Section 112, second paragraph, as being indefinite. The Official Action stated that the applicants claimed novelty due to the macrophage incubation medium used, but that this incubation medium is not stated in the claims set forth. The applicants respectfully traverse this rejection because the applicants' claims state that the macrophages have certain characteristics (i.e., increasing macrophage

cytotoxic activity by about 20 to 30% with respect to standard macrophages, etc.). These characteristics result from the applicants' method of manufacturing macrophages in the special incubation medium. The claims are intended to include macrophages with the same characteristics, manufactured by another method, not yet discovered.

Item 5 of the Official Action rejected claims 3-5 under Section 102(b) as being anticipated by CHOKRI et al. 1992. The Official Action stated that the macrophages in the applied article showed an increase in cytotoxic activity within the range of this claimed invention, when they were administered in conjunction with bispecific antibodies. In response, we are claiming macrophages cultivated in a way that, without bispecific antibodies being attached to macrophages, the macrophages alone exhibit increased cytotoxic activity.

Item 5 of the Official Action further stated that the applied CHOKRI article teaches precoating the macrophages with bispecific antibodies and simultaneous administration of macrophages and bispecific antibodies. The applied article does, indeed, teach precoating differentiated macrophages with bispecific antibodies, but this is a different step than what is claimed in the present invention, which has antibodies in the incubating step. The

incubating step is the stage when the monocytes differentiate into macrophages in a culture medium. Incubating macrophages in the presence of antibodies is a different process than precoating macrophages with antibodies. Incubating in the presence of antibodies increases FcγR1 expression and therefore increases cytotoxicity. The idea of adding bispecific antibodies into a culture medium when the monocytes are differentiating into macrophages is novel and not taught or suggested in the article.

Item 6 of the Official Action originally rejected former claims 1 and 2 under Section 102(e) as being anticipated by U.S. Patent 5,635,600 (FANGER et al.) and thereafter applied the rejection to claims 3-5. The applied reference discloses macrophages treated with interferon gamma and conjugated with bispecific antibodies to treat cancer. This reference, however, does not teach about the macrophages by themselves, but in conjunction with bispecific antibodies. FANGER et al. do not teach increasing the macrophage's cytotoxicity without the bispecific antibody coating. Macrophages that are, by themselves, 20 to 30% more cytotoxic than standard macrophages is not taught or suggested by FANGER et al. and, therefore, the applicants' claims are not anticipated.

Item 7 of the Official Action rejected claims 3-5 under Section 102(b) as being anticipated by WO 91/05871 (Medarex). This reference describes cultivating monocytes in a culture medium in order to differentiate the monocytes into macrophages. Reconsideration and withdrawal of the rejection are respectfully requested for the following reason: The applied reference does not teach or claim deriving macrophages in such as way as to increase the cytotoxicity of these macrophages by 20 to 30% over standard macrophages. The reference does not, furthermore, teach or suggest using the same special culture medium to incubate the monocytes in order to achieve macrophages with an increased cytotoxicity over standard macrophages.

Evidence that the prior art's macrophages do not, alone, exhibit especially high cytotoxicity can be found in claim 18a, which merely claims "an effector cell expressing high affinity Fc-γ receptor". An effector cell (i.e., macrophage), expressing Fc-γ receptors indicates the effector cell is cytotoxic. It is not novel for a macrophage to express Fc-γ receptors, but this applied reference does not teach or suggest macrophages with an increase in cytotoxicity compared to standard macrophages (which may be indicated by an increased expression of Fc-γ receptors). It merely describes an effector cell with

cytotoxic activity as a potential host to bispecific antibodies. Therefore, WO 91/05871 does not anticipate the present invention.

In light of the arguments discussed above, applicant believes that the present application is in condition for allowance.

If the Examiner has any questions or requires clarification, the Examiner may contact the undersigned attorney so that this application may continue to be expeditiously advanced.

Respectfully submitted,

YOUNG & THOMPSON

By _____ 7/19/01

Andrew J. Patch
Attorney for Applicants
Registration No. 32,925
745 South 23rd Street
Arlington, VA 22202
Telephone: 703-521-2297

July 27, 2001